

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A cell adhesion modulating agent that
 - (a) inhibits desmosomal cadherin-mediated cell adhesion; and
 - (b) consists essentially of a linear peptide having the amino acid sequence Arg-Trp-Ala-Pro-Ile-Pro (SEQ ID NO: 2).
2. (Canceled)
3. (Withdrawn) The cell adhesion modulating agent of claim 1 wherein the agent comprises the Trp-containing cell adhesion is present within the ring of a cyclic peptide.
4. (Withdrawn) The cell adhesion modulating agent of claim 3 wherein the size of the ring is from 6 to 15 amino acids.
- 5.-7. (Canceled)
8. (Withdrawn) The cell adhesion modulating agent of claim 3 wherein the Trp-containing cell adhesion recognition sequence is selected from the group consisting of Arg-Trp-Ala-Pro-Ile-Pro, Glu-Trp-Ile-Lys-Phe-Ala, Glu-Trp-Val-Lys-Phe-Ala, and Ala-Trp-Ile-Thr-Ala-Pro.
9. (Canceled)
10. (Currently Amended) The cell adhesion modulating agent of claim 1 wherein the peptide comprises an N-terminal or C-terminal modification sequence consisting

essentially of the amino acid sequence Arg-Trp-Ala-Pro-Ile-Pro (SEQ ID NO: 2) is C-terminal carboxylate esterified or amidated.

11. (Currently Amended) The cell adhesion modulating agent of claim ~~40~~1 wherein the ~~N-terminal modification is N-acetylation~~sequence consisting essentially of the amino acid sequence Arg-Trp-Ala-Pro-Ile-Pro (SEQ ID NO: 2) is N-acetylated.

12.-13. (Canceled)

14. (Original) The cell adhesion modulating agent of claim 1 linked to a solid support.

15. (Canceled)

16. (Withdrawn) The cell adhesion modulating agent of claim 1 further comprising an antibody or antigen-binding fragments thereof that specifically binds to a cell adhesion recognition sequence other than SEQ ID NO: 1 or SEQ ID NO: 2.

17. (Withdrawn) The cell adhesion modulating agent of claim 1 further comprising

(a) a cell adhesion recognition sequence other than SEQ ID NO: 1 or SEQ ID NO: 2 wherein the cell adhesion recognition sequence is separated from SEQ ID NO: 1 or SEQ ID NO: 2 by a linker, and

(b) an antibody or antigen-binding fragments thereof that specifically binds to a cell adhesion recognition sequence other than SEQ ID NO: 1 or SEQ ID NO: 2.

18. (Original) A composition comprising a cell adhesion modulating agent of claim 1 in combination with a physiologically acceptable carrier.

19. (Withdrawn) A method for modulating cell adhesion, comprising contacting a cell that expresses a desmosomal cadherin with a cell adhesion modulating agent of claim 1 and thereby modulating cell adhesion.

20. (Withdrawn) The method according to claim 19, wherein the cell is an epithelial cell.

21. (Withdrawn) The method according to claim 19, wherein the cell is a tumor cell.

22. (Withdrawn) The method according to claim 19, wherein the desmosomal cadherin is desmoglein 1, desmoglein 2, desmoglein 3, desmoglein 4, desmocollin 1, desmocollin 2, desmocollin 3, and desmocollin 4.

23. (Withdrawn) The method according to claim 19, wherein the cell adhesion modulating agent inhibits desmosomal cadherin-mediated cell adhesion.

24. (Withdrawn) The method according to claim 19, wherein the cell adhesion modulating agent enhances desmosomal cadherin-mediated cell adhesion.

25. (Withdrawn) A method for reducing the progression of a cancer in a mammal, comprising administering to a mammal having a cancer a modulating agent according to claim 1 and thereby reducing the progression of the cancer in the mammal, wherein the modulating agent inhibits desmosomal cadherin-mediated cell adhesion.

26.-38. (Canceled)

39. (Withdrawn) A method for screening a candidate compound for the ability to modulate desmosomal cadherin-mediated cell adhesion, comprising comparing a three-

dimensional structure of a candidate compound to a three-dimensional structure of a peptide comprising an amino acid sequence as set forth in SEQ ID NO: 1 or SEQ ID NO: 2 and a cell adhesion modulating activity, wherein similarity between the structure of the candidate compound and the structure of the peptide is indicative of the ability of the candidate compound to modulate desmosomal cadherin-mediated cell adhesion, and therefrom evaluating the ability of the candidate compound to modulate desmosomal cadherin-mediated cell adhesion.

40. (Withdrawn) A method for identifying a compound that modulates desmosomal cadherin-mediated cell adhesion, comprising:

(a) determining a level of similarity between a three-dimensional structure of a candidate compound and a three-dimensional structure of a peptide comprising an amino acid sequence as set forth in SEQ ID NO: 1 or SEQ ID NO: 2 and a cell adhesion modulating activity; and

(b) identifying an alteration in the structure of the candidate compound that results in a three-dimensional structure with an increased similarity to the three-dimensional structure of the peptide; and therefrom identifying a compound that has the ability to modulate desmosomal cadherin-mediated cell adhesion.

41. (Withdrawn) A method for evaluating a peptidomimetic for the ability to modulate desmosomal cadherin-mediated cell adhesion, comprising:

(a) culturing cells that express an desmosomal cadherin in the presence and absence of a peptidomimetic, under conditions and for a time sufficient to allow cell adhesion, wherein the peptidomimetic has a three-dimensional structure that is substantially similar to a three-dimensional structure of a peptide having an amino acid sequence as set forth in SEQ ID NO: 1 or SEQ ID NO: 2 and a cell adhesion modulating activity; and

(b) visually evaluating the extent of cell adhesion among said cells, and therefrom identifying a peptidomimetic capable of modulating cell adhesion.

42. (Withdrawn) A method for evaluating a peptidomimetic for the ability to modulate desmosomal cadherin-mediated cell adhesion, comprising:

(a) contacting an epithelial surface of skin with a test marker in the presence and absence of a peptidomimetic, wherein the peptidomimetic has a three-dimensional structure that is substantially similar to a three-dimensional structure of a peptide having an amino acid sequence as set forth in SEQ ID NO: 1 or SEQ ID NO: 2 and a cell adhesion modulating activity; and

(b) comparing the amount of the test marker that passes through said skin in the presence of the peptidomimetic to the amount that passes through skin in the absence of the peptidomimetic, and therefrom determining whether the peptidomimetic modulates cell adhesion.

43. (Withdrawn) A process for manufacturing a compound that modulates cell adhesion comprising

- (a) performing the method according to claim 39 or claim 40; and
- (b) producing the compound identified in step (a).

44. (Withdrawn) A process for manufacturing a peptidomimetic that modulates cell adhesion comprising

- (a) performing the method according to claim 41 or claim 42; and
- (b) producing the peptidomimetic if the peptidomimetic has the ability to modulate desmosomal cadherin-mediated cell adhesion.

45. (Withdrawn) A cell adhesion modulating agent that

- (a) modulates atypical cadherin-mediated cell adhesion; and
- (b) comprises
 - (i) a Trp-containing cell adhesion recognition sequence of an atypical cadherin molecule, but contains no more than 14 consecutive amino acid

residues present within the atypical cadherin molecule; wherein the Trp-containing cell adhesion recognition sequence is

A) the amino acid sequence Gly/Asp/Ser-Trp-Val/Ile/Met-Trp-Asn-Gln (SEQ ID NO: 5), wherein Gly/Asp/Ser is an amino acid selected from the group consisting of Gly, Asp and Ser, and Val/Ile/Met is an amino acid selected from the group consisting of Val, Ile and Met, or

B) the amino acid sequence Ala-Trp-Val-Ile-Pro-Pro (SEQ ID NO: 6);

(ii) a conservative analogue of SEQ ID NO: 5 or SEQ ID NO: 6;

(iii) an antibody or antigen-binding fragment thereof that specifically binds to SEQ ID NO: 5 or SEQ ID NO: 6; or

(iv) a peptidomimetic of SEQ ID NO: 5 or SEQ ID NO: 6.

46. (Withdrawn) The cell adhesion modulating agent of claim 45 wherein the Trp-containing cell adhesion recognition sequence is present within a linear peptide.

47. (Withdrawn) The cell adhesion modulating agent of claim 45 wherein the Trp-containing cell adhesion recognition sequence is present within the ring of a cyclic peptide.

48. (Withdrawn) The cell adhesion modulating agent of claim 47 wherein the size of the ring is from 6 to 15 amino acids.

49. (Withdrawn) The cell adhesion modulating agent of claim 45 wherein the agent is a peptide ranging in size from 6 to 50 amino acid residues.

50. (Withdrawn) The cell adhesion modulating agent of claim 49 wherein the agent is a peptide ranging in size from 6 to 15 amino acid residues.

51. (Withdrawn) The cell adhesion modulating agent of claim 46 wherein the Trp-containing cell adhesion recognition sequence is an amino acid sequence selected from the group consisting of Gly-Trp-Val-Trp-Asn-Gln (SEQ ID NO: 1353), Asp-Trp-Ile-Trp-Asn-Gln (SEQ ID NO: 1354), Ser-Trp-Met-Trp-Asn-Gln (SEQ ID NO: 1355), Ser-Trp-Val-Asn-Gln (SEQ ID NO: 1356), Gly-Trp-Met-Trp-Asn-Gln (SEQ ID NO: 1357), and Ala-Trp-Val-Ile-Pro-Pro (SEQ ID NO: 6).

52. (Withdrawn) The cell adhesion modulating agent of claim 47 wherein the Trp-containing cell adhesion recognition sequence is an amino acid sequence selected from the group consisting of Gly-Trp-Val-Trp-Asn-Gln (SEQ ID NO: 1353), Asp-Trp-Ile-Trp-Asn-Gln (SEQ ID NO: 1354), Ser-Trp-Met-Trp-Asn-Gln (SEQ ID NO: 1355), Ser-Trp-Val-Asn-Gln (SEQ ID NO: 1356), Gly-Trp-Met-Trp-Asn-Gln (SEQ ID NO: 1357), and Ala-Trp-Val-Ile-Pro-Pro (SEQ ID NO: 6).

53. (Withdrawn) The cell adhesion modulating agent of claim 45 wherein the cell adhesion modulating agent is a peptide comprising SEQ ID NO: 5 or SEQ ID NO: 6, or a conservative analogue of SEQ ID NO: 5 or SEQ ID NO: 6.

54. (Withdrawn) The cell adhesion modulating agent of claim 53 wherein the peptide comprises an N-terminal or C-terminal modification.

55. (Withdrawn) The cell adhesion modulating agent of claim 54 wherein the N-terminal modification is N-acetylation.

56. (Withdrawn) The cell adhesion modulating agent of claim 45 linked to a heterologous compound.

57. (Withdrawn) The cell adhesion modulating agent of claim 56 wherein the heterologous compound is a pharmaceutically active compound.

58. (Withdrawn) The cell adhesion modulating agent of claim 45 linked to a solid support.

59. (Withdrawn) The cell adhesion modulating agent of claim 45 further comprising a cell adhesion recognition sequence other than SEQ ID NO: 5 or SEQ ID NO: 6 wherein the cell adhesion recognition sequence is separated from SEQ ID NO: 5 or SEQ ID NO: 6 by a linker.

60. (Withdrawn) The cell adhesion modulating agent of claim 45 further comprising an antibody or antigen-binding fragments thereof that specifically binds to a cell adhesion recognition sequence other than SEQ ID NO: 5 or SEQ ID NO: 6.

61. (Withdrawn) The cell adhesion modulating agent of claim 45 further comprising

(a) a cell adhesion recognition sequence other than SEQ ID NO: 5 or SEQ ID NO: 6 wherein the cell adhesion recognition sequence is separated from SEQ ID NO: 5 or SEQ ID NO: 6 by a linker, and

(b) an antibody or antigen-binding fragments thereof that specifically binds to a cell adhesion recognition sequence other than SEQ ID NO: 5 or SEQ ID NO: 6.

62. (Withdrawn) A composition comprising a cell adhesion modulating agent of claim 45 in combination with a physiologically acceptable carrier.

63. (Withdrawn) A method for modulating cell adhesion, comprising contacting a cell that expresses a cadherin with a cell adhesion modulating agent of claim 45 and thereby modulating cell adhesion.

64. (Withdrawn) The method according to claim 63, wherein the cell is selected from the group consisting of vascular smooth muscle cells, endothelial cells, neural cells, obstoblast cells, and tumor cells.

65. (Withdrawn) The method according to claim 63, wherein the cadherin is selected from the group consisting of cadherin-5, cadherin-6, cadherin-7, cadherin-8, cadherin-9, cadherin-10, cadherin-11, cadherin-12, cadherin-14, cadherin-15, cadherin-19, cadherin-20, and PB cadherin.

66. (Withdrawn) The method according to claim 63, wherein the cell adhesion modulating agent inhibits cadherin-mediated cell adhesion.

67. (Withdrawn) The method according to claim 63, wherein the cell adhesion modulating agent enhances cadherin-mediated cell adhesion.

68. (Withdrawn) A method for reducing the progression of a cancer in a mammal, comprising administering to a mammal having a cancer a modulating agent according to claim 45 and thereby reducing the progression of the cancer in the mammal, wherein the modulating agent inhibits cadherin mediated cell adhesion.

69.-93. (Canceled)

94. (Withdrawn) A method for screening a candidate compound for the ability to modulate cell adhesion, comprising comparing a three-dimensional structure of a candidate compound to a three-dimensional structure of a peptide comprising an amino acid sequence as set forth in SEQ ID NO: 5 or SEQ ID NO: 6 and a cell adhesion modulating activity, wherein similarity between the structure of the candidate compound and the structure of the peptide is indicative of the ability of the candidate compound to modulate atypical cadherin-

mediated cell adhesion, and therefrom evaluating the ability of the candidate compound to modulate cell adhesion.

95. (Withdrawn) A method for identifying a compound that modulates cell adhesion, comprising:

(a) determining a level of similarity between a three-dimensional structure of a candidate compound and a three-dimensional structure of a peptide comprising an amino acid sequence as set forth in SEQ ID NO: 5 or SEQ ID NO: 6 and a cell adhesion modulating activity; and

(b) identifying an alteration in the structure of the candidate compound that results in a three-dimensional structure with an increased similarity to the three-dimensional structure of the peptide; and therefrom identifying a compound that has the ability to modulate cell adhesion.

96. (Withdrawn) A method for evaluating a peptidomimetic for the ability to modulate cell adhesion, comprising:

(a) culturing neurons on a monolayer of cells that express atypical cadherin in the presence and absence of a peptidomimetic, under conditions and for a time sufficient to allow neurite outgrowth, wherein the peptidomimetic has a three-dimensional structure that is substantially similar to a three-dimensional structure of a peptide having an amino acid sequence as set forth in SEQ ID NO: 5 or SEQ ID NO: 6 and a cell adhesion modulating activity;

(b) determining a mean neurite length for said neurons; and

(c) comparing the mean neurite length for neurons cultured in the presence of peptidomimetic to the neurite length for neurons cultured in the absence of the peptidomimetic, and therefrom determining whether the peptidomimetic modulates cell adhesion.

97. (Withdrawn) A method for evaluating a peptidomimetic for the ability to modulate cell adhesion, comprising:

- (a) culturing cells that express an atypical cadherin in the presence and absence of a peptidomimetic, under conditions and for a time sufficient to allow cell adhesion, wherein the peptidomimetic has a three-dimensional structure that is substantially similar to a three-dimensional structure of a peptide having an amino acid sequence as set forth in SEQ ID NO: 5 or SEQ ID NO: 6 and a cell adhesion modulating activity; and
- (b) visually evaluating the extent of cell adhesion among said cells, and therefrom identifying a peptidomimetic capable of modulating cell adhesion.

98. (Withdrawn) A method for evaluating a peptidomimetic for the ability to modulate atypical cadherin-mediated cell adhesion, comprising:

- (a) contacting an epithelial surface of skin with a test marker in the presence and absence of a peptidomimetic, wherein the peptidomimetic has a three-dimensional structure that is substantially similar to a three-dimensional structure of a peptide having an amino acid sequence as set forth in SEQ ID NO: 5 or SEQ ID NO: 6 and a cell adhesion modulating activity; and
- (b) comparing the amount of the test marker that passes through said skin in the presence of the peptidomimetic to the amount that passes through skin in the absence of the peptidomimetic, and therefrom determining whether the peptidomimetic modulates cell adhesion.

99. (Withdrawn) A method for evaluating the ability of a peptidomimetic to modulate atypical cadherin-mediated cell adhesion, comprising:

- (a) contacting a blood vessel with a peptidomimetic, wherein the peptidomimetic has a three-dimensional structure that is substantially similar to a three-dimensional structure of a peptide having an amino acid sequence as set forth in SEQ ID NO: 5 or SEQ ID NO: 6; and

(b) comparing the extent of angiogenesis of the blood vessel to a predetermined extent of angiogenesis observed for a blood vessel in the absence of the peptidomimetic, and therefrom determining whether the peptidomimetic modulates cell adhesion.

100. (Withdrawn) A process for manufacturing a compound that modulates cell adhesion comprising

- (a) performing the methods according to claim 94 or claim 95; and
- (b) producing the compound identified in step (a).

101. (Withdrawn) A process for manufacturing a peptidomimetic that modulates cell adhesion comprising

- (a) performing any one of the methods according to claims 96-99; and
- (b) producing the peptidomimetic if the peptidomimetic has the ability to modulate atypical cadherin-mediated cell adhesion.

102. (New) A cell adhesion modulating agent that

- (a) inhibits desmosomal cadherin-mediated cell adhesion; and
- (b) consists essentially of four or five amino acid residues of the sequence Arg-Trp-Ala-Pro-Ile-Pro (SEQ ID NO: 2).